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EXAMINER

GILLESPIE, BENJAMIN

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1-6, 8-9, 15-18, 20-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over English et al ('691). English et al teach a bioabsorbable tissue adhesive comprising polyester and aromatic diisocyanates, with the polyester backbone preferably derived from lactide, glycolide, and ϵ -caprolactone and initiated by 1,1,1-tris (hydroxy-methyl)ethane or ethylene glycol (Col 2 lines 60-68; col 3 lines 1-19). In particular patentees explain that the aromatic diisocyanate is present in excess by as much as a 6:1 NCO:OH ratio (Col 7 lines 63-65). Therefore, although not explicitly stated the reaction system contains isocyanate-terminated prepolymers but also additional diisocyanate monomer.
2. Although English et al teach that the bio-absorbable polyesters may be based on di or tri functional compounds, patentees fail to teach a polyurethane system that is a mixture of both. Nevertheless it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Kerkhoven* 205 USPQ 1069.
3. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over English et al ('691) in view of Bennett et al ('130). Aforementioned, English et al teach a polyurethane adhesive comprising the reaction product of isocyanate-terminated bio-absorbable polyester prepolymers, and important to note is that English et al further teach said adhesive may contain

catalyst such as 1,4-diazabicyclo [2,2,2] octane, however there is no disclosure correspond to applicants' cure time of claim 23 (Abstract).

4. Bennett et al teach an adhesive comprising a (A) bio-absorbable oligomeric ester, (B) tri-functional compound, and (C) diisocyanate, wherein (A) and (B) are terminated with isocyanate groups (Abstract; col 3 lines 39-57; col 4 lines 37-60; col 5 lines 58-67). Important to note is that Bennett et al teach the adhesive composition is cross-linked through the aid of 1,4-diazabicyclo[2.2.2]octane, at a temperature between 20°C and 40°C, and as little as five minutes (Col 6 lines 22-37).

5. Although Bennett et al specifies that the selection of diisocyanate is important and certain aromatic diisocyanate should not be employed because of toxicity concerns, it still would have been obvious to utilize the cross-linking parameters of Bennett et al in the composition of English et al based on the motivation that Bennett et al do not limit certain diisocyanates, and the composition of English et al has been clearly disclosed for use as a living tissue adhesive and therefore is safe for in-situ applications. Another important note is that the both teach 1,4-diazabicyclo[2.2.2]octane as the cure catalyst, wherein the curing takes place in at the same temperatures, and the reactive species present during cross-linking, i.e. isocyanate groups and water, are the same.

6. Claims 1-9, 13-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipatova et al ('535) in view of English et al ('691) and Ueyanagi et al ('245). Lipatova et al teach a tissue adhesive composition comprising bioabsorbable compounds that are end-capped with aromatic diisocyanate, and aromatic diisocyanate (Col 1 lines 33-48, 66-67). Specifically,

Art Unit: 1796

patentees explain the aromatic diisocyanate consist of 4,4'-diphenylmethane diisocyanate, naphthalene diisocyanate, and toluene diisocyanate (Col 2 lines 20-23).

7. Lipatova et al also teach a method of adhering a first and second tissue together via said composition, sealing a defect in tissue via said composition, wherein the seal prevents leakage of bodily fluids, and the composition is cross-linked through contact with water (Col 1 lines 24-26; col 4 lines 58-68; and col 9 lines 3-6). Still, patentees fail to teach bioabsorbable polyester that corresponds to applicants' claims and trifunctional adducts of the aromatic polyisocyanate.

8. Aforementioned, English et al teach bioabsorbable tissue adhesives comprising polyester and aromatic diisocyanates, with the polyester backbone preferably derived from lactide, glycolide, and ϵ -caprolactone and initiated by pentaerythritol or ethylene glycol (Col 2 lines 60-68; col 3 lines 1-19). Patentees go on to explain that these polymers have the advantage of acting as normal constituents in metabolic pathways after being broken down by hydrolysis, and therefore are less toxic to the user (Col 2 lines 18-22).

9. Therefore it would have been obvious to one of ordinary skill in the art at the time of invention to utilize the polyesters of English et al in Lipatova et al based on the motivation that both teach bioabsorbable tissue adhesives based on polyester backbones and aromatic diisocyanates, and the polyester of English et al is less toxic for the user.

10. Ueyannagi et al teach adhesives containing tri-isocyanate functional urethane adducts of diisocyanate, which are the reaction product of tri-functional alcohols such as trimethylolpropane or glycerin and aromatic diisocyanate (Abstract; col 1 lines 5-17; col 3 lines 17-25; col 7 lines 38-40, 46-47; col 8 lines 47-50). Specifically, patentees explain that monomeric diisocyanate exhibit high viscosities thereby requiring the addition of organic solvent or heating in order to

obtain a level of adequate mixing prior to application. The urethane adduct overcomes this deficiency by inherently exhibiting a lower viscosity (Col 1 lines 19-68; col 2 lines 1-56).

11. Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to include tri-functional urethane adducts of aromatic diisocyanate as disclosed by Ueyannagi et al in Liptova et al based on the motivation that both are drawn to polyurethane based adhesives, the urethane adduct improves mixability without the addition of organic solvent, which is harmful in bio-applications, or pre-heating, which is undesirable because of excess pre-cure, and it is prima facie obvious to add a known ingredient for its known function; *In re Linder* 173 USPQ 356; *In re Dial et al* 140 USPQ 244.

12. Finally regarding the amounts of claims 13 and 14, although Liptova et al teach the polyester based urethane prepolymer may be present between 30 and 99% by weight of total composition, there is no teaching to as how much the diisocyanate monomer and adduct should be present. Nevertheless it would have been obvious to arrive at applicants' claimed ranges based on the presence of the adduct has an effect on the resulting viscosity of the polyurethane reaction system, i.e. the amount is a result effective variable, and it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977); *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Response to Arguments

13. Applicant's arguments filed 5/5/1008, with respect to the rejection of claim 15 under 35 U.S.C. 112 2nd paragraph has been considered and is persuasive; the rejection has been withdrawn.

14. Applicant's arguments filed 5/5/1008, with respect to the rejections of the claimed invention in view of the prior art has been considered but are not persuasive. In particular, patentees argue that:

- a. claims 1-6, 8-9, 15-18, 20-22, and 24 are patentable over English et al ('691), because English et al fail to teach the three required components consisting of isocyanate terminated bioabsorbable polyester, isocyanate-terminated trifunctional compound, and diisocyanate,
- b. claim 23 is patentable over English et al ('691) in view of Bennett et al ('130), because the teachings of Bennett et al are not relevant because patentees are not drawn to a bio-tissue adhesive, and
- c. claims 1-9, 13-22, and 24 are patentable over Lipatova et al ('535) in view of English et al ('691) and Ueyanagi et al ('245), because similar to English et al, Lipatova et al fail to teach all three required components, the isocyanate terminated bioabsorbable polymer is not the same as claimed, and the secondary references fail to remedy these deficiencies; the examiner disagrees.

15. Concerning issue **a**, the examiner would like to first point out contrary to applicants' assertions, the disclosed composition does in fact contain unreacted monomeric diisocyanate (emphasis added), which is clearly supported by the teachings of English et al. Specifically, column 7 line 63 to column 8 line 39 explains monomeric diisocyanate is present in a 6:1 molar excess, and said excess remains in the system and participates in "curing." By having a 6:1 molar excess of monomeric diisocyanate, less than 100% of the diisocyanate present in the

Art Unit: 1796

reaction system is consumed during the synthesis of the isocyanate-terminated bioabsorbable prepolymer, thereby making monomeric diisocyanate available in the adhesive system.

16. Regarding the position that English et al fail to teach both isocyanate terminated bioabsorbable polyester and isocyanate-terminated trifunctional compound, the examiner would like to redirect applicants' attention to paragraph 2 and the last sentence of paragraph 1 in the instant office action; the examiner has already acknowledged this deficiency. Patentees teach bioabsorbable compounds initiated with either di **or** tri functional initiator, thereby producing di **or** tri functional polyester polyol, which later capped with aromatic diisocyanate. It should be noted that isocyanate terminated polyester triol is taken to satisfy the "trifunctional compound that is end-capped with an aromatic diisocyanate," limitation of claim 1. Hence, while the examiner notes that English et al fail to teach a combination of the di and tri functional isocyanate-terminated compounds, applicants not set forth any type of argument as to why it would not have been obvious to combine these two species, as previously discussed in paragraph 2 and therefore the examiner maintains his position.

17. In response to issue **b**, while it is noted that the teachings of Bennett et al are not drawn to bio-tissue adhesives, the test of analogous prior art is twofold. First it is decided if the reference is within the field of the inventor's endeavor. If it is not, then it must be determined whether the reference is reasonably pertinent to the particular problem with which the inventor was involved. *In re Wood*, 202 USPQ 171, 174; *In re Clay*, 23 USPQ.2d 1058. Therefore, while Bennett et al may not be directed to the same endeavor as English et al, it still provides pertinent information regarding cure characteristics for compositions using analogous cure methods and catalysts, and as a result Bennett et al qualifies as relevant prior art.

18. Finally regarding issue **c**, applicants have not set forth any logic that shows why the presently claimed invention is patentable over the combination of teachings; applicants instead only discuss what each individual reference lacks and therefore appear to be arguing each reference solely and not in view of one another. The examiner reminds applicants that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co. Inc.*, 80 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). With this understanding, the examiner would like to remind applicants why the claimed invention has been rendered obvious by the prior art.

19. It is noted that Lipatova et al do not teach the same bio-absorbable polyester polyol, however **in view of** English et al, it would have been obvious to arrive at applicants' claimed composition because English et al teach it as preferred for bio-tissue adhesives. Furthermore, the examiner notes that Lipatova et al fail to teach tri-functional isocyanate-terminated compounds, however **in view of** Ueyannagi et al, it would have been obvious to arrive at applicants' claimed composition since Ueyannagi et al teach such trifunctional compounds decrease viscosity without the need for organic solvent, which would A) facilitate application of the adhesive and B) is necessary without solvent since it would be toxic to the user.

Conclusion

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

Art Unit: 1796

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN J. GILLESPIE whose telephone number is (571)272-2472. The examiner can normally be reached on 8am-5:30pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vasu Jagannathan can be reached on 571-272-1119. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rabon Sergent/
Primary Examiner, Art Unit 1796

Application/Control Number: 10/533,041
Art Unit: 1796

Page 10

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